

Frequency of complications and risk factors involve after therapeutic ERCP

UT Kyow¹, BC Das², MJK Bhuiyan³, T Talukdar⁴, MJG Uddin⁵

Abstract

Background: Endoscopic Retrograde Cholangio Pancreatography (ERCP) is an exclusive for both diagnostic and therapeutic modality for manage both biliary and pancreatic disease. But now it rarely use for diagnostic purpose due to development of noninvasive MRCP. Complications are rare but once it happens it may fatal. Therefore knowledge of common complications and risk factors for developing complication are essential for selection of patient. **Objective:** Understand the complications and factors involved in developing complication after therapeutic ERCP. **Study design:** Cross-sectional study. **Place of study:** Department of Surgery, BSMMU. **Period of study:** Jan. 2015 to Dec. 2015. **Methods:** one hundred and fifty-eight patients underwent therapeutic ERCP for different reasons within study period. Among them 18 patient denied to be included in the study. Rest 140 patients were included in this study and complications occurred in 23 patient. All respondent divided into 2 groups. One group-1 (n=117) belonged to those patients who manifested uneventful outcome labeled as 'patients without complications' and another group-2 (n=23) belonged to those patients who experienced different sorts of events labeled as 'patients with complication'. **Results:** Out of 140 patients 23(16.42%) experienced complications. Complication were Cholangitis 8(5.7%), pancreatitis 7(5.0%) patients as well as hemorrhage 7(5%), 1(0.7%) patient had perforation and 1(0.7%) patient died due to septicemia followed by multiorgan failure. Univariate analysis shows that History of acute pancreatitis prior ERCP, patient taking anti-platelet and anti-coagulant drugs, difficult cannulation, precut sphincterotomy are related to post ERCP complications (P<0.001). In multivariate analysis revealed that history of acute pancreatitis and precut sphincterotomy shows independent risk factors for development of complication. **Conclusion:** This study demonstrate that pancreatitis and cholangitis are most common complications after ERCP. Acute episodes of pancreatitis prior ERCP and precut sphincterotomy needing for cannulation of common bile duct are the risk factors for developing complications after ERCP.

Key words: ERCP, Cholangitis, Pancreatitis, septicaemia.

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Introduction

Endoscopic Retrograde Cholangio Pancreatography (ERCP), which is widely available for the diagnosis and treatment of pancreaticobiliary diseases, is one of the most complex endoscopic procedures. A reported complication rate after ERCP varies in between 5% to 10%¹. Precise identification of risk factors for ERCP complications is important for improving the safety of ERCP. ERCP was developed primarily as a diagnostic modality for

visualizing the biliary and pancreatic system and was first performed and described in 1968². Compared with other endoscopic examinations, ERCP carries a higher potential for complications that range from trivial incidents with prompt resolution to major life-threatening crises such as severe acute pancreatitis. Other complications include cholangitis, hemorrhage, perforation, cholecystitis, stent related complications, and cardiopulmonary complications³. The reported incidence of post-ERCP complications varies widely from study to study and ranges for pancreatitis between 1-5%, hemorrhage 1-4%, perforation 1-2% and cholangitis 1-5%⁴. Nevertheless, acute pancreatitis is the most common serious complication of ERCP. It accounted for more than one-half of complications of endoscopic sphincterotomy in two large series⁵. However, ERCP is one of the most technically demanding and the highest risk procedures performed by gastrointestinal endoscopists. Hence, it requires significant focused training and experience to maximize success and safety⁶. Therapeutic ERCP is the almost challenging procedure that may arise more complications than

1. Dr. U Than Kyow
Assistant Registrar (Surgery)
250 Bed District Sadar Hospital, Cox's Bazar.
2. Dr. Bidhan C. Das
Department of Surgery, BSMMU.
3. Dr. Mohammed Jahangir Kabir Bhuiyan
Associate Professor (Surgery)
Cox's Bazar Medical College.
4. Dr. Tutul Talukdar
Resident Surgeon.
250 Bed District Sadar Hospital, Cox's Bazar
5. Dr. Md. Jamshed Gias Uddin
Assistant Registrar (Surgery)
250 Bed District Sadar Hospital, Cox's Bazar.

Correspondence :

Dr. U Than Kyow
e-mail: uthankyow@yahoo.com

diagnostic ERCP for its complex approach. It has proven to be a successful and durable solution in the treatment of patients with various operable and inoperable conditions related to hepatobiliary and pancreatic system. In many studies the clinical outcome of therapeutic ERCP showed excellent results. Since 1974 endoscopic management of bile duct stone has become the approach of choice, especially after cholecystectomy and in-patient with high surgical risk. Now the advantage of therapeutic ERCP over open surgery makes it predominant method of treating choledocholithiasis⁵. Several series have shown that 85-90 % of common bile duct stones can be effectively removed by ERCP⁷. Malignancy of the pancreas, gall bladder or bile ducts is also cause of biliary obstruction. Surgery is the standard treatment but unfortunately only 20% are operable. Patients with malignancies of the biliary tree have a poor prognosis; obstruction to bile flow can lead to severe symptoms and ultimately to liver failure⁸. Stent placement is associated with lower procedure related mortality, complications and shorter hospital stay when compared with surgical procedures. Complication like cholangitis develops due to inadequate drainage, incorrect stent position, migration and early obstruction. Polydorou et al., reported cholangitis in 7% of their cases in 1991⁹. Numerous factors have been found to correlate with the development of post ERCP cholangitis and pancreatitis. Some of these are patient specific (eg, age, sex, history of PEP), whereas others are procedure specific (eg, pancreatic sphincterotomy, precut sphincterotomy) or endoscopist experience. Freeman et al, in their study recognized some important risk factors that are intimately related to post ERCP cholangitis and pancreatitis. These are –Balloon dilatation of biliary sphincter, History of post ERCP pancreatitis, normal bilirubin, Pancreatic duct injection, Pancreatic sphincterotomy, Precut sphincterotomy, suspected sphincter of Oddi dysfunction and young age group people¹⁰. Besides, factors such as endoscopist's experience and timing of precut may affect the risk, although the literature is mixed. The recognized risk Factors for cholangitis identified as significant include the use of combined percutaneous-endoscopic procedures, stent placement in malignant strictures, the presence of jaundice, primary sclerosing cholangitis, low case volume, and incomplete or failed biliary drainage. Complication after therapeutic ERCP threatened the life. For this

causes identification of risk factors those responsible for post ERCP complication is essential. Although many data on this ground available world wide but no such data published from our country. The reason why this study is under taken to understand the complication after therapeutic ERCP and risk factors involve in developing complication in our perspective.

Materials And Methods :

This study was prospective cross sectional study, within the period of September 2015 to February 2016. This study is designed to be conducted among those patients who attending for therapeutic ERCP in surgery ward of BSMMU, Dhaka. Patients were subject to selection, all patients 18 years and above of both sexes, all patients who underwent ERCP procedures for therapeutic purpose, ASA grade I, II and III, Patients who wishes to be included in the study after explanation. On other side patients with history of pancreatobiliary surgery in last 6 months, pregnancy, pancreatitis before procedure, patients on corticosteroids, Those who do not wish to be included in the study and moribund patients are excluded. By purposive sampling 158 number of patient was selected for this study. Information collected by active participation, by interviewing through preformed structured questionnaires, by interviewing of operating surgeon, by proper clinical evaluation of postoperative period like history taking, clinical examination and relevant investigations, blood biochemistry (serum amylase, CBC, Serum bilirubin, prothrombin time, serum alkaline phosphatase, SGPT, SGOT etc), and ultrasonography. All data was checked and edited after collection. Chart by spread sheet of Windows 7. Frequency distribution and normal distribution of all continuous variables was calculated by mean and standard deviation like age, hospital stay etc. Cross tabulation was prepared and a comparison was made between the respondents from different age, sex, co morbidities, underlying pathology. Data processing and analysis was done by help of SPSS version 17 and 'P' values <0.05 was considered as statistically significant. On ethical implication no sensitive question was asked during the experiment, ethical clearance was taken from the IRB of BSMMU. The procedure was explained to the sample unit and they was informed that if they do not wish to be included in the study it will in no way hamper the treatment of their patient and at any point of the study, if they wish, they can withdraw themselves from the study at any

moment. Informed written consent of the patient was taken. Study outcome variable are patient's demographic profile, indication of ERCP, Procedure performed (sphincterotomy, CBD stenting, stone extracton, precut sphincterotomy, Pancreatic duct contrast injection and transpancreatic sphincterotomy), Difficult CBD cannulation, Previous H/O post ERCP cholangitis and pancreatitis, types of complications and types of drugs used for associated diseases. Expert opinion was taken from specialists of the Department of Surgery, Hepatobiliary Surgery, Critical Care and from Bio statisticians

Result:

The present study was conducted to understand the complication after therapeutic ERCP and factors involve in developing complication. In the study, 158 patients were selected first on the basis of clinical diagnosis and selection criteria using the purposive sampling method. Among these patients, 18 patients did not give consent to be included in the study. So, ultimately 140 patients were included. Among them, 117 patients showed uneventful outcome and rest 23 showed therapeutic ERCP related complications. These population were grouped into 'patients without complication' and 'patients with complication'. A pre-structured data collection sheet was used to receive data from patients. The data were collected, edited, gathered, plotted into tabular and figure form. Odds ratio and 95% Confidence interval were determined. Chi square test, univariate and multivariate analysis were done. p value was set as significant when it was <0.05. The results and observations are shown below. In total number of respondent age range was 18-81 years, of them 18-59 years age group where 35 patient and >60 age group where 105 patient. Mean age of the patient was 43.78±10.29 years and there were 120 males and 20 females patient. Analysis of demographic variables between patients without complications and with complications showed that 20% of patients with the age between 18 to 59 years old developed complications and patient with age more than 60 years, 15.2% patients developed complications. Regarding sex, 15.8% male patients and 20% female patients developed complication after ERCP. 16% of patients with malignant diseases and 14.4% patients with benign diseases developed complications after therapeutic ERCP. The interesting finding was that the 50% patients who had previous history of acute pancreatitis and took Antiplatelet/ NSAID developed complications after

ERCP. The patients of having associated disease 13.1% patients developed complications.

Table I : Differences of demographic variables between patients without and with complications.

Without complication	With complication	
Age (years)		
18-59	28(80%)	7(20%)
>60	89(84.76%)	16(15.24%)
Sex		
Male	101(84.17%)	19(15.84%)
Female	16(80%)	4 (20%)
Disease		
Malignancy	42(84%)	8(16%)
Benign	77(85.5%)	13(14.4%)
H/O acute pancreatitis	2(50%)	2(50%)
Associated disease		
(DM, HTN, COPD, CAD, CVD)	16(80%)	8(13.11%)
Drugs		
Antiplatelet/ NSAID	6(50%)	6(50%)
Anticoagulant	3(75%)	1(25%)

DM : Diabetic mellitus

HTN : Hypertension

COPD : Chronic obstructive pulmonary disease

CAD : Coronary artery disease

CVD : Cerebral vascular diseases

In procedure related variables, maximum group of patient 62(44.29%) perform sphincterotomy with stenting but complication shows high in percentage 5(62.5%) in group of sphincterotomy with stone extraction and stenting. In procedure details shows easy canulation possible in maximum respondent 67(47.87%) but complication higher in difficult cannulation and precut group.

Table II : Difference of procedure related variable between patient without complications and with complications

	Without complication	With complication
Procedure details		
Easy canulation	63(94.02%)	4(5.97%)
Difficult canulation	45(81.81%)	10(18.29%)
Precut sphincterotomy	15(83.34%)	3(16.67%)
Procedure perform		
-Only sphincterotomy	23(92%)	2(8%)
-Sphincterotomy with stenting	52(83.87%)	10(16.12%)
-Sphincterotomy, stone extraction	39(86.67%)	6(13.33%)
-Sphincterotomy, stone extraction and CB stenting	3(37.5%)	5(62.5%)

Out of 140 patients, Complications occurred in 23(16.43%) patients after therapeutic ERCP

procedure. Common complications were cholangitis in 5.7% (n=8) patients, haemorrhage in 5.0% (n=7), pancreatitis in 7 (5.0%) and duodenal perforation in 1 (0.71%). Patient survived who had duodenal perforation after laparotomy and repair of perforation. One of 8 patients who had cholangitis died of septic shock and multiple organ failure because of uncontrolled infection

Table III : distribution of the complications (n=140)

Complication type	number	percentage
Morbidity		
-pancreatitis	7	5.0%
mild acute pancreatitis	5	3.5%
severe acute pancreatitis	2	1.42%
Bleeding	7	5.0%
Intraprocedural	6	4.2%
Immediate	1	0.07%
Delayed	0	0%
Cholangitis	8	5.7%
Perforation	1	0.71%
Mortality	1	0.71%
Total =	23	(16.43%)

Table IV : Risk factors for overall complications after therapeutic ERCP in univariate analyses(n=23)

Univariate analysis

Risk factors	All procedures (N=140)	Overall complication (N=23)	P-value	Odds ratio	95%CI
Age <60 y	35	7	NS	0.68	0.43-4.39
History of acute pancreatitis	4	2	<0.001 ^S	2.87	1.76-4.65
Prior cholecystectomy	94	12	NS	1.12	0.69-2.89
Female gender	20	4	NS	0.87	0.51-2.89
NSAID or aspirin/clopidogrel use	12	6	0.03 ^S	1.59	1.06-2.86
Anticoagulant use	4	1	0.03 ^S	1.88	1.29-3.92
Difficult cannulation	55	10	0.005 ^S	2.32	1.21-4.42
Suspected SOD	4	1	<0.001 ^S	0.79	0.25-1.75
Precut access sphincterotomy	18	3	<0.001 ^S	1.92	1.27-4.62
Needle-knife	15	3	0.005 ^S	1.64	1.25-2.81
Transpancreatic sphincterotomy	3	0	NS	1.95	1.19-3.37

CI : confidence interval;
 NSAID :non-steroid anti-inflammatory drug
 SOD :sphincter of Oddi dysfunction
 S : Significant
 NS : Not Significant

In univariate analysis of risk factors shows that history of acute pancreatitis, use of NSAID/ Clopidogral and anti-coagulant, difficult cannulation, suspected SOD and precut sphinterotomy have significant relation(P=<0.001^S).

But in multivariate analysis shows only history of acute pancreatitis, difficult canulation and precut sphinterotomy have significant relation with development of complication(<0.001^S).

Table V : Risk factors for overall complications after therapeutic ERCP in multivariate analyses (n=23)

Multivariate analysis

Risk factors	All procedures (N=140)	Overall complication (N=23)	P-value	Odds ratio	95%CI
Age <60 y	35	7			
History of acute pancreatitis	4	2	<0.001 ^S	2.29	1.49-3.69
Prior cholecystectomy	94	12			
Female gender	20	4			
NSAID or aspirin/clopidogrel use	12	6	NS	0.95	0.66-2.33
Anticoagulant use	4	1	NS	1.14	0.74-2.97
Difficult cannulation	55	10	<0.001 ^S	2.05	1.17-3.83
Suspected SOD	4	1	NS	0.79	0.25-1.75
Precut access sphincterotomy	18	3	<0.001 ^S	1.89	1.15-4.22
Needle-knife	15	3	0.005 ^S	1.64	1.25-2.81
Transpancreatic sphincterotomy	3	0	NS	0.95	0.75-2.79

CI : confidence interval;
 NSAID : non-steroid anti-inflammatory drug
 SOD : sphincter of Oddi dysfunction
 S : Significant
 N : Not Significant

Discussion :

Magnetic resonance cholangiopancreatography (MRCP), multidetector helical CT, and endoscopic ultrasound are replacing diagnostic ERCP day by day¹¹. In contrast, since its introduction forty years ago, therapeutic ERCP continues to remain an essential therapeutic modality for a variety of biliary and pancreatic diseases. Over the last 2 decades significant advances have been made in ERCP, i.e. intensive training, novelties in accessories (hydro philic guide wires¹², steerable catheters, diathermy with microprocessors), which facilitate the cannulation of a desired duct, and contribute to controlled cutting of ampullary sphincter, minimizing the trauma of major papilla. However, the incidence of post-ERCP complications has not changed during last ten years¹³.

Therefore, identifying patient and procedure-related risk factors for post-ERCP complications has a significant impact on clinical practice helping in the implementation of appropriate pharmacological¹⁴ and technical measures(pancreatic stents, ES via hydrophilic guide wire to avoid the “zipper cut” phenomenon) to reduce the likelihood of post-ERCP complications¹⁵.

Moreover, the assessment of risk factors allows better identification of patients who might be candidates for immediate discharge after therapeutic ERCP and might reduce the financial cost of the procedure.

A number of prospective and retrospective multicenter studies have investigated patient and procedure related risk factors of therapeutic ERCP¹⁶. Result of our study little differs from

previous studies, because of our therapeutic endoscopist works in a more challenging atmosphere.

Univariate and multivariate analysis showed history of acute pancreatitis (ERCP or non-ERCP-related) as the only patient-related risk factor for overall complications and PEP this finding is consistent with previous studies¹⁷.

Others patient demographic factors like -Younger age (<60 years), female sex and anatomical abnormality periampullary diverticulum were not associated risk factors for overall complications. Although these three patient-related parameters were reported in earlier studies as risk factors for PEP and post-ES bleeding and perforation¹⁷ but more recent studies and multivariate analysis did not consider these parameters *per se* as risk factors for post-ERCP complications¹⁸. So, this result also consistent with our study.

Technical variables are of obvious importance as procedure-related factors in overall post-ERCP complications and especially PEP. It is interesting that when visualization is limited to the main pancreatic duct, the risk is not significant. These findings confirm the hypothesis that hydrostatic injury from pancreas overfilling is the main trigger of activation of PEP mechanism.

Precut access papillotomy in this study was a significant risk factor for overall complications and especially for PEP, this finding is similar with previous studies and meta-analyses¹⁷. It is interesting that when analyzing the influence of the three subtypes of precut access papillotomy, we found that NKP and TPS on both analyses were significant risk factors for PEP. Contrary to this finding, in this study we did not found any complication after TPS, although sample is small and we mention it as one of our study limitation. In this precut access papillotomy thermal injury and subsequent edema are major cause of development of complication.

Difficult cannulations were also risk factors for PEP by both analyses, which was same as most studies and meta-analyses recorded them as independent predictors of PEP¹⁹. But SOD not as previous study, This difference is explained by the fact that SOD diagnosis in our study was based on clinical and laboratory findings (Milwaukee criteria) and not on sphincter of Oddi manometry. We acknowledge this as a limitation of our study since all our patients were SOD I or SOD II. In these patients the pathogenesis of SOD is probably related to stenosis resulting from passive obstruction at the sphincter of Oddi caused by fibrosis, inflammation, or both. Dyskinesia of the sphincter, which results from intermittent

obstruction caused by sphincter muscle spasm, is more common in patients with SOD III. Patients with suspected SOD III but no manometric confirmation were not included in this study and these are the SOD patients that are at greater risk for PEP.

Moreover, it is a common belief that papillary trauma from repeated attempts to achieve selective bile duct cannulation leads to edema with a subsequent major impact on sphincter hypertension-related impairment of pancreatic drainage and PEP development²⁰. Papillary trauma occur in different way, when the cannulation is attempted by a trainee or an endoscopist with low experience or a very experienced endoscopist.

Although in a recent study covered and uncovered self-expanding metal stent placement (SEMS) was reported as a risk factor for PEP²¹, in the present study we only found significant association when simultaneously done sphincterotomy with stone extraction and stent placement.

In case of Post-ERCP complication- bleeding, pancreatitis and cholangitis were observed commonly same as previous studies¹⁸, with most bleedings being intraprocedural. But frequency of complication are little higher than previous, we consider it may be due to low volume case and adverse environment.

We examined as risk factors for post-ES hemorrhage the use of oral anticoagulants and aspirin/clopidogrel, precut access papillotomy with its subtypes and the presence of periampullary diverticulum. Although univariate analysis showed aspirin/clopidogrel and anticoagulant use as risk factors for post-ES bleeding, on multivariate analysis which has more credibility, no relationship was found between the use of drugs influencing the platelet's function or coagulation cascade and post-ES hemorrhage. The guidelines of the European Association of Gastrointestinal Endoscopy (ESGE) recommend that aspirin and other NSAIDs should be continued in patients undergoing ES, especially in patients at high risk of thromboembolic events, because the risk of bleeding is not different between patients with/without their use. However, the recommendations are less clear regarding the use of clopidogrel in endoscopic interventions²².

Conclusion:

The observations here demonstrate that pancreatitis and cholangitis are most common complications after ERCP. Acute episodes of pancreatitis prior ERCP and precut sphincterotomy needing for cannulation of common bile duct are the risk factors for developing complications after ERCP.

Limitation of this study was- it was a cross sectional, single center, short period study and

sample size also small.

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